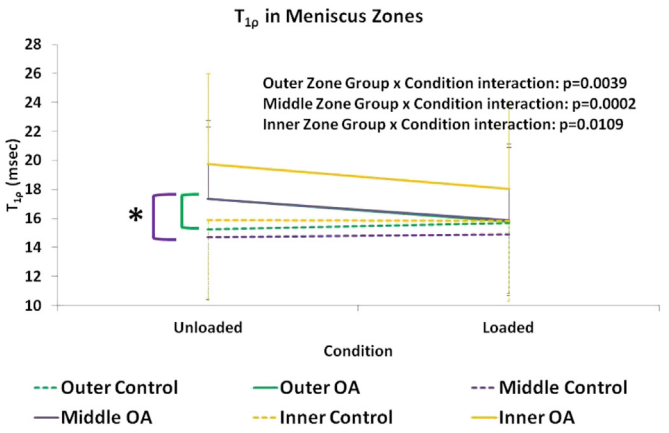


Fig. 3. T1ρ changes with loading in the three posterior horn medial meniscus zones for control and OA groups. *Signifies P < 0.05.

to understand the mechanism underlying these differences and their effect on OA progression. This work was funded by NIH-NIAMS RO1 AR046905.

## 443
## QUANTITATIVE MEASURES OF MENISCUS EXTRUSION PREDICT INCIDENT RADIOGRAPHIC KNEE OSTEOARTHRITIS-DATA FROM THE OSTEOARTHRITIS INITITATIVE

K. Bloecker †‡, E. Quinn §, J. Niu §, W. Wirth ‖†, F. Eckstein ‖†, D. Felson §. †*Paracelsus Med. Univ., Salzburg, AUSTRIA;* ‡*Dept. of Orthopeadics, BHS Linz, Linz, AUSTRIA;* §*Clin. Epidemiology Res. & Training Unit, Boston Univ. Sch. of Med, Boston, MA;* ‖*Chondrometrics GmbH, Ainring, GERMANY*

**Purpose:** Meniscal tears are highly prevalent in the general population and represent a risk factor for the onset and progression of knee osteoarthritis (KOA). Meniscus extrusion (subluxation) has been frequently observed in patients with KOA, and semi-quantitative MRI measures of extrusion (e.g. WORMS, BLOKS, MOAKS) have been identified as important predictors of structural progression over time (i.e. cartilage loss). We have recently developed quantitative measurement technology to determine meniscus size, shape, and position, relative to the tibial plateau cartilage. The objective of this study was to test the hypothesis that the above measures predict incident radiographic KOA, prior to the advent of radiographic evidence of disease.

**Methods:** 4796 Osteoarthritis Initiative participants were enrolled at four clinical sites. We studied the knees exhibiting incident radiographic KOA (on central readings of fixed flexion radiographs). These were defined as knees with Kellgren Lawrence grade (KLG) 0 or 1 at baseline that developed a combination of a definite osteophyte and OARSI joint space narrowing (JSN) grade $\geq$ 1 by year 4 (Y4) follow up. These knees were matched by baseline KLG0/KLG1 frequency (~30%/70%) to control knees that did not develop incident KOA. 438 case or control knees had coronally reconstructed double echo steady state (DESSwe) MR images, which were previously validated in the context of quantitative extrusion measurements. The tibial, femoral and external surfaces of the medial (MM) and lateral meniscus (LM) were segmented in the central 5 slices of the tibia. Proprietary software (Chondrometrics GmbH, Ainring, Germany) was used to determine quantitative measures of meniscus size and position in this region of interest. Case and control knees were compared using conditional logistic regression adjusting for age, sex, BMI, race and clinical site. To address whether meniscal changes existed well before OA development, we performed sensitivity analyses; excluding incidence in the first 2 years after baseline.

**Results:** Of 206 knees with incident radiographic KOA, 75% had medial and 25% lateral JSN at follow-up; 64% had incidence at Y1/2, and 36% at Y3/4 follow-up. 134 incident cases were female (age 61.5 y, BMI 28.9 kg/m$^2$) and 72 male (61.4; 29.4). Of 232 non-incident knees, 141 were female (age 61.4 y, BMI 27.5 kg/m$^2$) and 91 male (60.4; 27.7). In the baseline images, the mean extrusion distance between the tibial and medial meniscus (MM) margin in the central 5 slices was 1.56 ± 1.12 mm (mean ± SD) in knees with incident radiographic KOA, vs. 1.29 ± 0.99mm in non-incident knees (+21%, adj. odds ratio (OR) per standard deviation 1.35 [95% CI 1.10,1.65; p < 0,01]). No significant difference was noted in lateral meniscus (LM) extrusion. Similar observations were made for the percent area of the MM extruding the tibial cartilage medially (TA uncov%; Table 1). Further, knees with incident radiographic KOA displayed greater medial and lateral meniscus volume (Vol). Other measures of meniscus size (width, height, surface areas) were consistently greater in incident vs. non-incident knees, but the differences did not reach statistical significance (data not shown). The percent coverage of the medial (MT Cart cov%) and lateral tibia (LT Cart cov%) was similar between incident and non-incident knees (Table 1). The differences were attenuated when the analysis was restricted to only those with incident KOA at Y3/4, but still reached significance for MM TA uncov% (data not shown). The results were very similar when restricting the analysis to the 77% with just medial incidence of KOA; however, the differences between incident and nonincident knees in (mean and maximal) medial meniscus thickness became significant (i.e. greater in knees with incident medial KOA; p < 0.01), whereas no differences were noted laterally.

**Conclusions:** Greater medial meniscus extrusion and greater meniscus volume, predict incident radiographic KOA. However, tibial coverage by the meniscus did not differ significantly between incident and non-incident knees. Greater medial meniscus thickness (height) predicts incident medial KOA, suggesting that meniscus hypertrophy/swelling is a sign of early KOA that precedes radiographic change in the same compartment.

Means + SD for meniscus measures incident vs. non-incident knees (Adj.OR = adjusted odds ratio per SD)

| | Incident Mean ± SD | Non-incident Mean ± SD | Diff % | Adj. OR (95% CI) | p-value |
|---|---|---|---|---|---|
| MM TA uncov % | 25.8 ± 15.8 | 22.0 ± 13.5 | 17.2% | 1.33 (1.08,1.64) | 0.007 |
| LM TA uncov% | 5.1 ± 7.8 | 4.5 ± 6.2 | 13.5% | 1.12 (0.91,1.36) | 0.281 |
| MM Vol | 222.6± 71.9 | 210.0 ±59.3 | 6.0% | 1.33 (1.06,1.67) | 0.014 |
| LM Vol | 294.4 ± 75.0 | 279.4 ± 59.0 | 5.4% | 1.36 (1.09.1.69) | 0.007 |
| MT Cart cov% | 22.6 ± 8.5 | 22.7 ± 6.9 | −0.4% | 0.99 (0.80,1.21) | 0.891 |
| LT Cart cov% | 32.0 ± 8.6 | 30.6 ± 7.4 | 4.7% | 1.17 (0.95,1.43) | 0.131 |

## 444
## DELAYED GADOLINIUM-ENHANCED MRI OF CARTILAGE (DGEMRIC) IS SUPERIOR TO T1RHO-MAPPING IN MEASURING CARTILAGE SULPHATED GLYCOSAMINOGLYCAN CONTENT: PRELIMINARY RESULTS OF AN IN-VIVO VALIDATION STUDY USING AN EX-VIVO REFERENCE STANDARD FOR CARTILAGE SULPHATED GLYCOSAMINOGLYCAN CONTENT

J. van Tiel, G. Kotek, M. Reijman, P.K. Bos, E.E. Bron, S. Klein, J.A. Verhaar, G.P. Krestin, H. Weinans, E.H. Oei. *Erasmus MC, Univ. Med. Ctr., Rotterdam, Netherlands*

**Purpose:** Quantitative radiological techniques for cartilage composition have become of interest to non-invasively diagnose knee osteoarthritis (OA) in an early disease stage, to follow subtle disease progression over time, and to assess the efficacy of potential novel treatment strategies for OA. An example of such a technique is delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) which has become a standard to quantitatively measure cartilage composition in terms of its sulphated glycosaminoglycan (sGAG) content. A drawback of dGEMRIC is the use of a contrast agent and the need for a long delay between contrast administration and MRI acquisition. T1rho-mapping has been proposed as non-contrast-enhanced alternative to dGEMRIC to quantitatively measure cartilage sGAG content. However, no thorough validation

studies comparing both techniques acquired in-vivo in one patient against a tissue reference standard for sGAG have been performed. The aim of this study was to assess the correlation of in-vivo dGEMRIC and T1rho-mapping outcomes in osteoarthritis patients with cartilage sGAG content determined using an ex-vivo reference standard.

**Methods:** We analyzed data of 12 patients from an ongoing study in which knee OA patients (Kellgren and Lawrence grade 2–4) undergo dGEMRIC and T1rho-mapping at 3T before total knee replacement (TKR). T1- and T1rho-values of both scans were calculated in 6 cartilage regions (medial and lateral weight-bearing (WB) femoral condyles and tibial plateaus and non WB cartilage of the condyles) (Fig. 1). Femoral and tibial cartilage was harvested during TKR and rescanned with contrast-enhanced microCT (CE-uCT), which served as reference standard for sGAG since it has been shown to accurately measure sGAG content. We analyzed the correlation between T1- and T1rho-values and CE-uCT outcomes with linear regression.

**Results:** T1- and T1rho-values ranged between 280–834 ms and 31–53 ms for dGEMRIC and T1rho-mapping respectively throughout the tibiofemoral knee joint. dGEMRIC outcomes had a strong negative correlation with reference CE-uCT X-ray attenuation, representing sGAG content of articular cartilage in the femoral cartilage ($r = -0.75$; $p < 0.0001$; 95%CI= -0.86 - -0.58), in the tibial cartilage ($r = -0.71$; $p < 0.0003$; 95%CI = −0.88–−0.41) and in the tibiofemoral cartilage ($r = -0.72$; $p < 0.0001$; 95%CI = −0.83–−0.58) (Fig. 2A). T1rho outcomes did not correlate with cartilage sGAG content of articular cartilage in the femoral cartilage ($r = 0.02$; $p = 0.91$; 95%CI= −0.30–0.33), in the tibial cartilage ($r = -0.09$; $p = 0.70$; 95%CI = −0.53–0.38) and in the tibiofemoral cartilage ($r = -0.03$; $p = 0.85$; 95%CI = −0.28–0.24) (Fig. 2B).

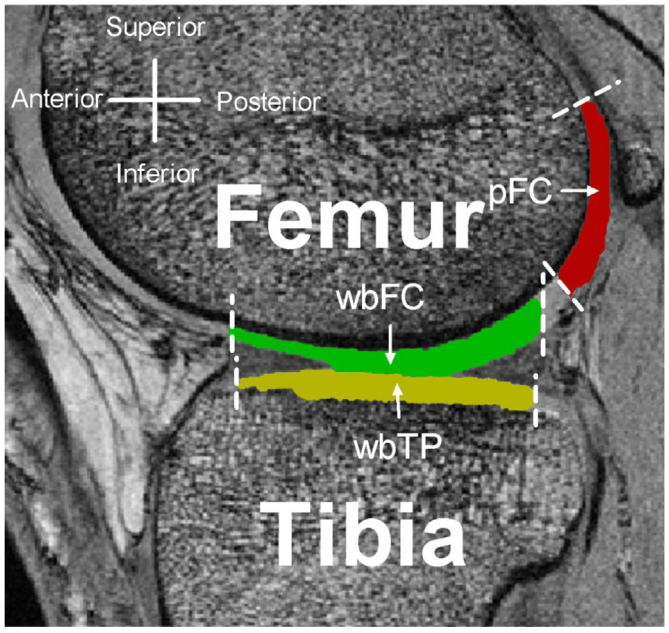


Fig. 1. Cartilage regions of interest in which outcomes of dGEMRIC, T1rho-mapping and contrast-enhanced microCT were analyzed.

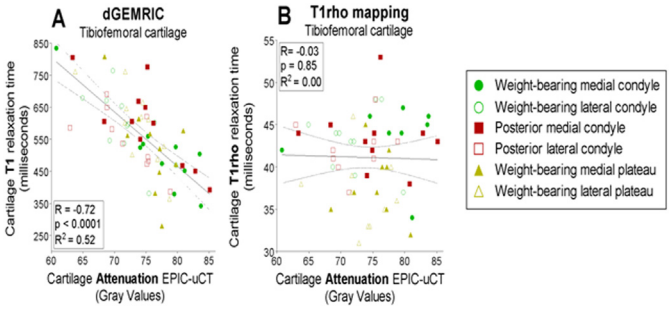


Fig. 2. Correlation plot of outcomes of dGEMRIC and contrast-enhanced microCT (A) and correlation plot of outcomes of T1rho-mapping and contrast-enhanced microCT (B) in the tibiofemoral joint. The dashed lines represent the 95% confidence interval of the linear regression.

**Conclusions:** Our preliminary results suggest that dGEMRIC can accurately measure articular cartilage sGAG content, whereas T1rho-mapping is not suitable for this purpose. Therefore, despite the need to use a contrast agent, we consider dGEMRIC to be superior to T1rho-mapping for quantitatively measuring cartilage sGAG content.

## 445
## SEX RELATED DIFFERENCES IN MRI FEATURES BETWEEN TWO ETIOLOGICALLY DIFFERENT OSTEOARTHRITIS SUBPOPULATIONS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

R. Roze, S.M. Bierma-Zeinstra, E.H. Oei, J.H. Waarsing. *Erasmus MC, Rotterdam, Netherlands*

**Purpose:** The observed heterogeneity in osteoarthritis with respect to e.g. risk factors, symptoms, affected joints and progression, gave rise to the idea that OA is in fact a collection of distinct disease subtypes. In this study we explored whether two etiologically distinct subtypes of knee OA with equal radiological OA severity, differ in osteoarthritis features as seen on MRI. The subtypes comprised a group with metabolic syndrome and a group of lean physically active subjects.

**Methods:** From all subjects of the Osteoarthritis Initiative (OAI) incidence subcohort, who had a KL score $\geq 2$ in at least one knee at 48 months follow-up, we included two groups of 50 subjects, matched for KL score. To be included in the metabolic syndrome group subjects needed to have a BMI $> 30$ kg/m$^2$ or abdominal circumference $>94$ cm for males or $>80$ cm for females. Further, 2 out of 3 of the following criteria needed to be present: hypertension (RR $> 130/85$ mmHg or use of hypertension medication), insulin resistance (reported high blood sugar or use of diabetic medication) or dyslipidemia (use of lipid lowering medication). Inclusion criteria for the physically active lean group were a BMI $< 25$ kg/m$^2$ and a Physical activity scale for the elderly (PASE) score $\geq 2$, which indicates strenuous sport/recreation activities. MRI scans made at 48 month follow-up were requested for these subjects from the OAI database, and one randomly selected OA knee from each subject was scored using the MRI Osteoarthritis Knee Score (MOAKS).

**Results:** The metabolic syndrome group consisted of 28 females and 22 males with an average age of 63.4 years while the physically active lean group consisted of 37 females and 13 males with an average age of 61.3 years. Scores for bone marrow lesions (BMLs), and cartilage damage were consistently higher in most of the knee compartments in the metabolic syndrome group, but only for females and only significant for cartilage damage. In the lateral tibia, however, scores for BMLs and cartilage damage were lower in the metabolic syndrome group, for both sexes. Osteophyte scores were higher for all compartments in the metabolic syndrome group, irrespective of sex, though these differences were only significant for a few compartments in females (see Fig.). Scores of meniscal tears and Hoffa synovitis were significantly higher in the physically active lean group while high prepatellar signal was more often seen in the metabolic syndrome group, especially in the females.

**Conclusions:** Metabolic OA and OA related to physical activity showed clear differences in MRI OA features, depending on sex and knee compartment. Intriguing is the difference between men and women in the pattern in which cartilage damage and BMLs are distributed over the compartments (see Fig.). This is suggestive of differences in biomechanics of the knee between the sexes, which have been shown to underlie the higher prevalence of patello-femoral problems in women. The fact that metabolic syndrome is associated with worse scores in women but not in men might be attributed to differences in fat distribution. Fat in females is deposited mostly subcutaneously, while males have more visceral fat. The subcutaneous amount of fat is related to leptin levels, and interestingly, leptin levels have been shown to influence OA, especially in women. Another interesting finding is that osteophyte scores behave differently than scores for BMLs and cartilage damage, in that the distribution over the compartments is less pronounced, and that scores are higher in the metabolic syndrome group, for both sexes. This suggests that the etiological process for osteophyte development is at least partly independent from the processes that influence cartilage damage and BMLs. In conclusion, these results suggest that different etiological processes in knee OA do lead to differences in structural degradation, which is probably modulated by biomechanical loads in the different compartments of the knee.